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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/727,628	12/01/2000	Katherine Armstrong	50,597	4194

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EXAMINER
KUBELIK, ANNE R

ART UNIT	PAPER NUMBER
1638	3

DATE MAILED: 03/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No.	Applicant(s)	
	09/727,628	ARMSTRONG ET AL.	
	Examiner	Art Unit	
	Anne Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the corr spondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-11 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-11 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claims 1-11 are pending.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-5 and 7-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a promoter of bases 7-2064 of SEQ ID NO:3, does not reasonably provide enablement for promoters that comprise fragments or variants of bases 7-2064 of SEQ ID NO:3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to a multitude of nucleic acids comprising myo-inositol-1-phosphate (MIP) synthase promoters, fragments of bases 7-2064 of SEQ ID NO:3 as small as 20 nucleotides, variants of bases 7-2064 of SEQ ID NO:3 or DNAs that hybridize to those bases, DNA constructs comprising those nucleic acids, plants transformed with those DNA constructs, and a method of using an ADF promoter to express a heterologous nucleic acid in a plant.

The instant specification, however, only provides guidance for the isolation of the MIP synthase cDNA from maize embryo cDNA by PCR with primers based on the yeast gene sequence and the use of the cDNA to probe a maize cDNA library (Example 1), analysis of MIP synthase expression patterns in maize seed (Example 2), cloning of the flanking sequences from maize genomic DNA and their sequencing (Example 3), and operable linkage of the *gus* coding

sequence to the full-length version of this isolated MIP synthase promoter (bases 7-2064 of SEQ ID NO:3) and in transient expression of GUS in maize embryos and stable expression in maize callus and plants (examples 3-7).

The instant specification fails to provide guidance for which nucleotides of bases 7-2064 of SEQ ID NO:3 can be altered and to which other nucleotides, and which nucleotides must not be changed, to maintain promoter and expression enhancing activity, respectively, in the variant DNAs. The specification also fails to provide guidance for which nucleotides can be deleted, or for how to make the deletions, to produce the claimed fragments and still produce a functional promoter or enhancer.

Twenty base-pair long regions of a DNA fragment that has promoter activity cannot predictably be assumed to also have promoter activity. Deletion analysis of various promoters have shown that even DNA segments from the portion of a promoter region containing sequence elements thought to be most important (*e.g.*, the TATA-box) need to be longer than 20 basepairs. Maiti et al, in studies on a figwort mosaic virus promoter, found that smallest portion upstream of the transcriptional start site of that would support transcription was 198 basepairs long; segments of 73 and 37 basepairs did not work (1997, Transgen. Res., 6:143-156, see Fig. 4).

Mutation of promoter sequences also produces unpredictable results. Donald et al (1990, EMBO J. 9:1717-1726) in a mutational analysis of the *Arabidopsis rbcS-1A* promoter found that the effect of a particular mutation was dependent on promoter fragment length (paragraph spanning pg 1723-1724).

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate a multitude of nucleic acids comprising MIP synthase promoters or fragments (including those as

small as 20 nucleotides) or variants of those nucleic acids. Making all possible 20 consecutive nucleotide fragments of bases 7-2064 of SEQ ID NO:3 would require generation and analysis of 2038 fragments, and making all possible single base variants would require making and analyzing 3^{2058} variants. The claims are drawn to variants that differ from bases 7-2064 of SEQ ID NO:3 by many more than a single base; thus, the actual number of variants to be analyzed greatly exceeds those numbers. The unpredictability discussed above suggests that none of the 20 base fragments would even function. Thus, without guidance, undue experimentation would be required to generate and analyze these fragments and variants.

Therefore, the specification is not enabled for a multitude of nucleic acids comprising MIP synthase promoters, fragments of bases 7-2064 of SEQ ID NO:3 as small as 20 nucleotides, variants of bases 7-2064 of SEQ ID NO:3 or DNAs that hybridize to those bases, DNA constructs comprising those nucleic acids, plants transformed with those DNA constructs, and a method of using an MIP synthase promoter to express a heterologous nucleic acid in a plant.

4. Claims 1-5 and 7-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a multitude of DNA molecules that comprise MIP synthase promoters from any source or that are variants of or "selectively hybridize" to bases 7-2064 of SEQ ID NO:3. In contrast, the specification only describes a nucleic acid from maize that comprises SEQ ID NO:3. Applicant does not describe other DNA molecules encompassed by the claims, and the structural features that distinguish all such nucleic acids from other nucleic acids are not provided.

Hence, Applicant has not, in fact, described DNA molecules that encode MIP synthase promoters or variants of bases 7-2064 of SEQ ID NO:3 within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

See *University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed, Cir. 1997):

> The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA .... Accordingly, the specification does not provide a written description of the invention ....

and at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

Claims 2-6 are indefinite in their recitation of "SEQ ID NO:2" as SEQ ID NO:2 is drawn to an amino acid sequence. For purposes of examination, it was assumed that the claims were drawn to SEQ ID NO:3, as this is what the specification states is the invention (see, *e.g.*, pg 7). Such treatment does not relieve Applicant of the responsibility to respond to this rejection.

Claims 2-3 are indefinite in their recitation of "fragment, genetic variant, or deletion". The similarity of the variant to bases 7-2064 of SEQ ID NO:3 are unclear. For purposes of examination, fragments as small as a single base, deletions of all except one base and variants having only one base in common with bases 7-2064 of SEQ ID NO:3 were assumed. Such treatment does not relieve Applicant of the responsibility to respond to this rejection.

The phrase "the ability of functioning" in claim 2 is not grammatically correct. It is suggested that it be replaced with --the ability to function--.

Claim 3 is indefinite for being dependent upon itself. For purposes of examination, it was assumed that the claim was dependent upon claim 2. Such treatment does not relieve Applicant of the responsibility to respond to this rejection.

In claim 3 it is suggested that the phrase "identical to ... defined by" be replaced with --of--.

In claim 4, it is not clear of the 20 base pair portion comprises 20 consecutive bases of bases 7-2064 of SEQ ID NO:3. For purposes of examination, it was assumed that the base pairs were not consecutive. Such treatment does not relieve Applicant of the responsibility to respond to this rejection.

In claim 4 it is suggested that the phrase "having a ... set forth in" be replaced with --comprising 20 consecutive base pairs of--.

Claim 5 is indefinite in its recitation of "selectively hybridizes". What hybridization conditions are considered "selective" are unclear. For purposes of examination, all conditions were assumed. Such treatment does not relieve Applicant of the responsibility to respond to this rejection.

Claims 1 and 7-8 are indefinite in their recitation of the abbreviation "MIP." For purposes of examination, it was assumed that "MIP" referred to "myo-inositol-1-phosphate." Such treatment does not relieve Applicant of the responsibility to respond to this rejection.

In claims 6 and 10-11, the article before "DNA" should be --the--.

Claims 7-8 are indefinite because they lack agreement between the preamble of the methods and the positive method steps. Method steps must be circular; the final step must generate the item the method is intended to produce. For example, the method of expressing a heterologous nucleic acid in a plant in claim 7 ends in regenerating a plant from a cell, when it should end in the expression of a heterologous nucleic acid in a plant. Similarly, the methods of claim 8 should end in the production of seed.

Claim 9 indefinite in its recitation of the word "including." It is unclear if this word is intended to be open or closed. If open language is intended, the word should be replaced with --comprising--.

Claim Rejections - 35.USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in-
(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

8. Claims 1-2, 4-5 and 7-11 are rejected under 35 U.S.C. 102(e) as being anticipated by Lappegard et al (US Patent 6,225,529, filed August, 1998).

Lappegard et al teach a nucleic acid with a 20 base pair contiguous region of bases 7-2064 of SEQ ID NO:2 and would thus comprise a fragment of bases 7-2064 of SEQ ID NO:2 (see sequence search results and claims 1, 4-5, 8-9, 12-13 and 15-33). This nucleic acid is a MIP synthase promoter (column 3, lines 1-5). This nucleic acid would also hybridize to bases 7-2064 of SEQ ID NO:2 and would be a variant of bases 7-2064 of SEQ ID NO:2 because it has 68.9% homology to bases 7-2064 of SEQ ID NO:2. Lappegard et al also teach plants and seeds transformed with constructs comprising the nucleic acid and a method of using it to express a heterologous nucleic acid in a plant seed (claims 23-33).

9. Claims 1-2 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Lopes et al (1991, Nucleic Acids Res. 19:1687-93).

Lopes et al teach a MIP synthase promoter (Figure 3) and DNA constructs comprising the promoter operably linked to the *lacZ* gene (Figure 1). This nucleic acid would also "selectively hybridize" to bases 7-2064 of SEQ ID NO:2 and would be a "genetic variant" of those bases.

10. Claims 3 and 6 are free of the prior art, given the failure of the prior art to teach or suggest a nucleic acid of bases 7-2064 of SEQ ID NO:2 or comprising at least 200 consecutive bases of bases 7-2064 of SEQ ID NO:2.

11. Claim 6 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst, Kimberly Davis, at (703) 305-3015.

Anne R. Kubelik, Ph.D.
March 11, 2002

Amy Nelson

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